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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,811	08/09/2001	Ivano Romano	029474-5006	6260
28977	7590	02/11/2004		
MORGAN, LEWIS & BOCKIUS LLP 1701 MARKET STREET PHILADELPHIA, PA 19103-2921			EXAMINER AKHAVAN, RAMIN	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,811	ROMANO ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30, 35-39, 43-59 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30, 35-39 and 43-59 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

This action is in response to applicant's amendment filed 11/14/2003. This action is non-final, as the newly made objections/rejections herein were not necessitated by amendments. Applicant has cancelled 31-34 and 40-42. Claims under consideration are 30, 35-39 and 43-59.

Response to Arguments

Applicant's arguments, see Remarks, filed 11/14/2003, with respect to objections/rejections made in Detailed Action, filed 08/12/2003 have been fully considered and are persuasive. Previously made objections and rejections have been withdrawn.

Applicant is correct that amendments narrowing claim 30 to disclosed species of the promoter sequence claimed (SEQ ID NO: 1) obviate the previous grounds of rejection under § 112 ¶ 1 rejection. Concomitantly the prior art rejection under § 102(b) is also obviated. Furthermore, applicant is correct that by submitting the certified translated copy of the foreign priority document (i.e. Swiss application (1999 0279/99) that the § 102 (a) rejection is obviated.

New Grounds for Objections and Rejections

Specification

The abstract of the disclosure is objected to because it exceeds 150 words. Correction is required. See MPEP § 608.01(b).

The disclosure is objected to because of the following informalities: There is no heading for the drawings (i.e. Brief Description of Drawings; See 37 CFR 1.77 (b)). Appropriate correction is required.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of CFR 1.821 through 1.825 because sequences set forth that lack sequence identifiers, no computer readable format (CRF) was filed, no paper sequence was filed and no attorney statement was filed. These sequences include those disclosed in Fig. 5. If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP § 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (See MPEP § 2422.02).

Applicant is required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 CFR 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

Claim Objections

Claims 30, 39, 47 and 56 are objected to because of the following informalities: Claim 30 contains an improperly dependant subpart, where subpart (d) is dependant from subpart (e). Claim 29 recites "STRE", but there is no preceding introduction as to what the acronym represents. Claims 47 and 56 contain an improperly capitalized "The". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30, 35-39 and 43-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- 1. Claim 30 recites “a” nucleic acid in subpart (a), when referring to “An isolated nucleic acid molecule comprising a heat inducible promoter...” in the preamble. There is insufficient antecedent basis for this limitation in the claim.**

It would be remedial to substitute “the” in place of “a” in subpart (a). In this way there would be proper antecedent basis with respect to the limitation in subpart (a) referring to the isolated nucleic acid recited in the preamble.

- 2. Claim 59 recites "a" heat-inducible promote in subpart (a). There is insufficient antecedent basis for this limitation in the claim.**

The same basis applies as in claim 30, because the limitation should be drawn to an already introduced element (i.e. heat-inducible promoter in claim 30's preamble), thus the proper article is “the” not “a”.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

- 3. Claim 30, 35-39 and 43-49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably**

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to nucleic acid molecules comprising a heat inducible promoter where in the nucleic acid molecule “hybridizes” with the complementary strand of the promoter sequence of the *H. polymorpha* gene encoding TSP or the nucleic acid sequence set forth in SEQ ID NO: 1. Therefore the claim is drawn to a genus of heat inducible promoters.

The written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure or by a combination of such identifying characteristics sufficient to show applicant was in possession of the claimed genus.

The specification does not contain any examples to support the genus claimed. It is noted that the specification characterizes “hybridizes” as being under a “stringent condition”, and provides an example. (Spec. p. 4, top). However, this “example” is only that and is not limiting to a particular set of conditions and as written, the claim is not limited with any regard to hybridization conditions. For example, in the extreme case, the claim would be drawn to any sequence comprising a heat inducible promoter that hybridizes, even if just for a moment.

In sum, there are an insufficient number of specific examples provided of the genus claimed to describe the genus. Furthermore, the claim does not contain critical limitations deemed necessary to apprise one of ordinary skill in the art, of the subject matter of which applicant is in possession. Therefore, it must therefore be considered that a representative

number of species sufficient to convince the skilled artisan that applicant is in possession of the claimed genus have not been disclosed.

It would be remedial to explicitly incorporate a set of stringent hybridization conditions for which there is literal support in the specification.

4. **Claims 44-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.**

The claims are drawn to SEQ ID NO: 6 or the trehalose-6-phosphate synthase (TSP) gene of *Hansenula polymorpha*, as well as polynucleotide or amino acid sequences with 80 or 90 percent identity to the TSP disclosed. Furthermore, the invention is drawn to any partial sequence of the TSP protein having synthase activity.

In short, the claims are drawn to genera of polynucleotide and polypeptide sequences. More specifically the claims are genus claims in terms of sequences with 80 percent, 90 percent or partial sequences thereof, viz., the *H. polymorpha* TSP disclosed. The specification does not contain any examples to support the genus claims. Nor is there any significant discussion of the structural/functional domains of the *H. polymorpha* TSP. Thus the disclosure is not descriptive of the complete structure of a representative number of species, which the claims encompass, as one of ordinary skill in the art cannot envision all the sequences claimed based on the teachings in the specification. In sum it must therefore be considered that a representative number of

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species sufficient to convince the skilled artisan that applicant is in possession of the claimed genus have not been disclosed.

5. **Claims 44-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for full length *H. polymorpha* trehalose-6-phosphate synthase (“TSP”; SEQ ID NOs: 6 and 7), does not reasonably provide enablement for sequences with 80 or 90 percent identity, or partial sequences of TSP. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.**

The test for enablement is whether one skilled in the art could make use the claimed invention from the disclosure in the specification coupled with information known in the art without undue experimentation. *United States v Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor but instead is a conclusion reached by weighing many factors which are outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). The factors include the following:

Scope/Breadth of the claims. The claims are broadly drawn to any polynucleotide or polypeptide sequence with 80 or 90 percent homology, or partial sequence of the TSP protein having synthase activity.

Nature of the invention. The invention is drawn to the *H. polymorpha* TSP gene, including the promoter region. More specifically, claims 44-46 are drawn to sequences sharing some identity (80 percent, 90 percent or partial sequence) with the TSP gene, while maintaining synthase activity.

Unpredictability of the art. There would be a great deal of unpredictability as to which protein regions or motifs would be necessary to preserve synthase activity. The skilled artisan would necessarily have to conduct trial and error experimentation to obtain the requisite information.

State of the art. The state of art is well developed. However, there would be required an input of substantial time and effort, to identify regions in the *H. polymorpha* TSP protein crucial for functionality, all of which would have to be done in an unpredictable, trial and error manner.

Amount of guidance provided. Applicant discloses the full-length protein. There is no guidance provided with regard to potential candidate sequences or regions, that would maintain synthase activity while sharing the recited identity with the disclosed sequence (i.e. SEQ ID NOs: 6 and 7). In short, the protein substructure has not been characterized, nor the sequence clarified, viz., functionality.

Number of working examples. Only the full length polynucleotide or polypeptide is disclosed (i.e. SEQ ID NOs: 6 and 7 respectively).

Level of Skill in the art. The level of skill in the art is high, however, given unpredictability in determining which sequences would preserve synthase function, the breadth of the claims and lack of guidance with respect to characterization of the TSP protein, it is considered that the skilled artisan would have had to have conducted undue, unpredictable

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experimentation in order to practice the claimed invention commensurate with the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 6. Claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Xiao-Dong Liu et al. EMBO, November 1, 1997, 16(21): 6466-6477 (hereinafter Xiao-Dong; provided to applicant in previous correspondence).**

Claim 30 is drawn to any sequence comprising a heat-inducible promoter wherein the promoter hybridizes with the complementary strand of a nucleic acid comprising the promoter of *H. polymorpha* gene having TSP activity or SEQ ID NO: 1. Because “hybridize” in this context can mean any sequence capable of hybridizing, even if just momentarily, then any isolated heat-inducible promoter under the right conditions could hybridize and thus read on the claim.

Xiao-Dong teaches a nucleic acid sequence for a human heat shock gene promoter element that is heat-inducible (p. 6471, column 2). In so far as the nucleic acid taught would be capable of hybridizing with the sequences claimed in 30(c), claim 30 is anticipated by the nucleic acid taught. This logically follows because an intrinsic quality of any sequence of DNA is that under the proper conditions it can hybridize with any other sequence of DNA, even if the two molecules share minimal sequence complementation. Therefore, an intrinsic quality of the

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sequence taught by Xiao-Dong would be that it would read on claim 30(c), as the sequence taught is for a heat-inducible promoter, which under proper conditions familiar to one of ordinary skill in the art at the time of the invention, would hybridize to the complementary sequence of 30(a) or (b).


Put another way, by delimiting the claim to the general condition of *hybridizing*, the claim language directs the invention to non-specific fragments of DNA. Therefore, as written, the claim is anticipated by Xia-Dong.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday- Friday from 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.


GERRY LEFFERS
PRIMARY EXAMINER